Ventilator-associated lung injury (VALI or VILI)

By Alex Yartsev - 16/06/2015
Last updated 04/11/2025 - 01:07

Question 11 from the second paper of 2003 touched on this topic. Specifically, the college wanted the trainees to talk about "volutrauma", which is only one aspect of VALI. Mechanisms of ventilator-associated lung injury in ARDS were also the subject of Question 10 from the first paper of 2012. Question 26 from the second paper of 2009 also discusses surgical emphysema as one of the consequences of barotrauma. In brief, VALI is cellular-level lung injury which occurs as the result of positive pressure ventilation. Its presentation is essentially indistinguishable from that of ALI and ARDS, but a characteristic ARSD-like picture does not need to form in every instance. Frequently, a degree of VALI underlies a syndrome of multiple organ system dysfunction, and contributes to it.

Alveolar overdistension: "volutrauma"

This is damage caused by over-distension. It is associated with inappropriately large volumes. For instance, back in the dark ages of ARDS management we used to ventilate people with 10-12ml/kg volumes, 700-800ml for your average sized male. We now know how wrong this was.

This is not a very intelligent concept. Essentially, each alveolus is a balloon. If you pump in enough gas, you will pop the balloon. The cellular consequences of alevolar overdistension are ruptured membranes, cellular death, failure of surfactant secretion, and the release of pro-inflammatory cellular contents.

basement membrane stretch and stress on intracellular junctions. Denuded collagen and leaking pneumocyte contents are highly immunogenic, and the ensuing inflammatory response lays waste the lung tissue, resulting in a familiar four-quadrant pattern of ARDS. All of this is bad if you are already short of working lung units.

This process is worst when there is heterogenous lung disease: the healthy lung will suffer the side effects of whatever ventilator strategy is being used to improve gas exchange within the diseased lung. Thus, huge tidal volumes are not required to induce this sort of lung injury.

The ultimate outcome of volutrauma may actually be macroscopic rather than microscopic. Pneumothorax and pneumomediastinum may develop as the alveoli rupture from overdistension.

Barotrauma

Increasing the transpulmonary pressures to above 50 cm H2O will cause disruption of the basement membranes and the destructive entry of pressurised airway gases into the parenchyma, or into blood vessels. The concept has existed since Mead et al (1970) modelled stress distribution in the lungs and arrived at the conclusion that even under relatively normal circumstances ventilation could apply truly ridiculous forces to vulnerable regions of a heterogeneously diseased lung. This arises from the fact that a pocket of collapsed lung that is surrounded by expanded air spaces on all sides is no longer being distended by transpulmonary pressure, as it can no longer see the pleural cavity. Instead it is being distended by the distending pressures applied by the surrounding structures, which Mead et al calculated to be related to transpulmonary pressure by the ratio of $(V/V_0)^{2/3}$, where V/V_0 is the difference in volume between the inflated and collapsed states of that little piece of lung. Considering that a lung can collapse down to about 8-10% of its original volume, this equation gives a multiplier of about 4.6, i.e. if the transpulmonary pressure was 25 cmH_2O, the distending pressure on this lung region would be an alveolus-cracking 115 cmH_2O.

Barotrauma and volutrauma may be functionally synonymous; even though one refers to excessive pressure and the other to excessive volume, in reality one cannot exist without the other. A situation where you cause trauma with large volumes *without* large pressures is inconcievable. Large pressures without large volumes are more the routine, but in that case the "volutrauma" definition still remains valid, as the alveoli are still being overdistended (its just that they break before they can distend to a large volume).

This is slightly different from the old, pre-1990s concept of ventilator barotrauma, which was a term applied in the olden days to any sort of lung injury due to a ventilator, and specifically to pnumothorax, pneumomediastinum and subcutaneous emphysema. To be sure, these are also complications to be wary of in the ARDS patient.

Barotrauma can be discussed as a separate issue to volutrauma because of the unique effects of excessive pressure on the lung. Pneumothoraces and pneumomediastinum are common to both volutrauma and barotrauma, but it is specifically barotrauma that causes air emboli (perhaps not in the setting of mechanical ventilation where pressures are measured in centimeteres, but in scubadiving where pressures are measured in *tens of meters*).

In spite of the frequency of serial re-examinations and chest Xrays in the ICU, you are usually alerted to the development of such a complication by the appearance of subcutaneous emphysema, as in Question 26 from the second paper of 2009. There are a few strategies for the management of subctaneous emphysema which are mentioned in that question, which go somewhat beyond the usual "Approach to the patient suddenly impossible to ventilate".

- Keep FiO2 high to aid in the resorption of surgical emphysema
- Consider subcutaneous Penrose drains or infraclavicular incisions down to pectoralis fascia to assist in the clearance of surgical emphysema (if it is posing a threat to the patient's stability, and only after surgcal consultation)
- Minimise positive pressure of ventilation if pneumothorax or bronchopleural fistula is implicated

It is rarely necessary to actually perform incisions, as subcutaneous emphysema will usually reabsorb on its own provided the air leak has been dealt with. However, it takes some time. If the patient is intubated already, you can usually afford to wait. Classically, the subcutaneous gas becomes a problem when it collects in the face (making extubation and reintubation impossible), or around the supraclavicular and suprasternal tissues (making percutaneous tracheostomy more difficult).

Alveolar cyclic atelectasis: "atelectotrauma"

The act of repeatedly inflating and collapsing tends to be stressful for alveoli, and the damage resulting from this causes a release of inflammatory cytokines. The damage can be observed in animal models. Experimental rabbits ventilated with high pressures but without PEEP were found to have more histological lung damage than ones ventilated with PEEP, which suggests that the extra damage was caused by the cyclical recruitment-derecruitment of lung units. Seems like this cyclical recruitment-derecruitment forms a significant part of VALI: "open-lung" ventilation improves the incidence of VALI by a significant amount, and it addresses precisely this mechanism.

In fact, a study from 2010 has shown that the benefit of high PEEP (preventing cyclic atelectasis) outweighs the harm from overdistension.

Macroscopic shear injury

Let us picture a region of atelectatic pus-filled lung which does not get any ventilation, and a region which is well ventilated. The well-ventilated region will expand and contract normally, and the atelectatic region will remain still sthroughout the respiratory cycle.

Now, imagine the alveoli at the junctioon between there two regions. With each breath, these lung units will find themselves grotesquely distorted, pulled every which way by the inflation of the good lung and the dead weight of the atelectatic lung.

The results can be demonstrated in experimental animals. The greatest amount of damage was around the borders of atelectatic regions. The authors of this amazing piece even made a condom model of the lung in order to better model their theories on lung unit interdependence.

Prone position ventilation may be protective against this, because the bases of lung (where shear injury tends to occur) remain more inflated.

Biotrauma

Mechanical ventilation is known to upregulate pulmonary cytokine production. When you injure the lung with violent ventilation, it fights back by flooding the

bloodstream with potent pro-inflammatory mediators. Remember that the lungs have the same volume circulating through them every minute as does the entire body. When this blood-filled sponge exudes toxic chemicals, they are rapidly blown all over the rest of your tissues, and there they wreak havoc. In extreme circumstances, this alone may be enough to cause multiorgan system failure.This confirms the observation that most ARDS patients die not of respiratory failure but of multi-organ dysfunction.

Release of these inflammatory mediators might occur by a variety of mechanisms:

- **Mechanotransduction:** alterations in cytoskeletal structure without any ultrastructural damage. Alveolar cells have stretch-activated ion channels and various other mechanical sensors. They may start to synthesise inflammatory mediators when these receptors and sensors are activated.
- **Decompartimentalisation:** stress failure of the alveolar barrier. In other words, broken alveolar cells, oozing with highly pro-inflammatory cellular content.
- **Necrosis:** dead alveolar cells obviously contribute to the inflammation
- **Pulmonary capillary endothelial dysfunction** related to stretch and vessel wall tension has the effect of adding to the inflammatory effect.

Oxygen toxicity

This is the damage caused by a high concentration of inspired oxygen. The influential NEJM article is behind a paywall, but there is something worth reading for free in Chest. And of course, as always with experiments regaarding the endurance by organisms of unnatural stresses, we have a study from the 1940s where ninety healthy young men were exposed to pure oxygen for prolonged periods.

After breathing a high (50% to 100%) concentration of oxygen, the first thing one will notice is tracheal irritation. Then, pleuritic pain and dyspnoea develops. On autopsy, individuals who died after prolonged hyperoxia were found to have lungs filled with haemorrhagic oedema, and there was widespread cytolysis histologically. Primates exposed to hyperoxia for up to 12 days were found to have their alveolar cells essentially destroyed after four days; by the end of their

exposure the alveoli had thickened walls with evidence of fibrosis, and a greatly reduced diffusing capacity.

Thus, targeting arterial normoxia in ARDS may actually contribute to worsening lung injury by the direct corrosive effects of oxygen. Though previously it was thought that the neurocognitive recovery of survivors might be improved by relatively high PaO_2 (80-110mmHg) these days we tend to be happy with a PaO_2 of 60 mmHg, corresponding to an SpO_2 of 90% or so.

Prevention and management of ventilator-associated lung injury

In summary:

Prevention of VALI

- Limit plateau airway pressure to under 30 cm H_2O
- Limit tidal volumes to 6ml/kg (4- 8ml/kg)
- Aim for lower oxygen levels, tolerate SpO_2 88-90%
- Use high PEEP (~15) to prevent cyclic atelectasis
- Use neuromuscular junction blockers (they improve mortality)
- Consider prone ventilation to protect against shear injury

Clinical manifestations of VALI

- Worsening gas exchange
- Increasing organ system failure due to cytokine release
- worsening lactic acidosis
- decreasing lung compliance
- pneumothorax
- pneumomediastinum
- surgical emphysema

Appropriate investigations

- CXR
- Plateau pressure measurement by inspiratory hold

Treatment of volutrauma

- Lung-protective ventilation (i.e. introduction of preventative measures if they weren't already in use)
- thoracocentesis for pneumothoraces
- dual-lumen intubation to isolate the affected lung, with the potential to ventilate it independently and a different pressure.

Keep the volumes low

Everybody knows. The ARDS Network data has confirmed that low tidal volumes improve survival; and it is postulated that it happens because of precisely this mechanism.

What if you don't have ARDS, but you are trying to prevent ventilator-induced ARDS? Nobody knows what the optimal tidal volume is, and it is generally assumed that 8ml/kg should be enough, but this has no evidence to support it.

Keep the PEEP high (but not too high)

Seems that in ARDS, the benefits of high PEEP outweigh the risks. Some say even 15cmH_2O is safe.

How high is high enough? This is open to debate. Some say it should be set at a level just above the lower inflection point of the pressure-volume curve (i.e. the point where the lung compliance suddenly increases). In practice, with heterogeneously diseased lungs, this point is difficult to find.

Also; in spite of the above assertion, if the plateau pressure is the same, decisions regarding PEEP (i.e. whether to have high PEEP or low PEEP) don't seem to have any influence on survival among ARDS patients.

Previous chapter: Outcomes in adult ARDS

Next chapter: Patient self-inflicted lung injury (P-SILI)

References

Most of this information comes from only two textbooks. With "Basic Assessment and Support in Intensive Care" by Gomersall et al (was well as whatever I picked up during the BASIC course) as a foundation, I built using the humongous and canonical "Principles and Practice of Mechanical Ventilation" by Tobins et al – the 1442 page 2nd edition.

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2013-2025